

The association of thrombocytopaenia and Lyme disease

Harold S. Ballard, Gino Bottino¹ and Joseph Bottino¹

Department of Medicine Department of Veterans Affairs Medical Center, 423 East 23rd Street, New York, NY 10010 and ¹North Westchester Medical Center, 400 East Main Street, Mt Kisco, New York, USA

Summary: The association of asymptomatic thrombocytopaenia in six patients with acute Lyme disease is described. Recovery from thrombocytopaenia occurred shortly following antibiotic therapy. Patients residing in endemic areas for Lyme disease who present with flu-like symptoms and laboratory findings of thrombocytopaenia should prompt suspicion of acute Lyme disease. Appropriate clinical studies should be undertaken to confirm the diagnosis.

Introduction

Lyme borreliosis is an arthropod-borne spirochaetal disease. Persons of all ages who engage in outdoor activities (occupational or recreational) are at risk. The highly endemic areas of North America are in Connecticut, New York, Massachusetts, New Jersey, Rhode Island, Minnesota and Wisconsin.¹ Exposure may be minimal, as in gardening or playing in the yard. The diagnosis of Lyme disease is based on the recognition of clinical features of the illness in a patient with a history of possible exposure to the causative organism (a bite from a spirochaete-laden hard tick of the genus *Ixodes*).¹ An early expanding skin lesion erythema chronicum migrans (ECM), is the clinical hallmark. In the early stage skin involvement is often accompanied by flu-like symptoms (malaise and fatigue, headache, fever and chills, myalgia and arthralgia).²

Thrombocytopaenia has not been reported in association with Lyme disease in the United States, although two patients with thrombocytopaenia and Lyme disease in Europe have been described.^{3,4} We report six patients in whom this association was noted (Table I).

Patients

Case 1

A 26 year old construction worker on a road gang sought medical attention because of a one week history of rash, fever, aching joints and severe headaches. Physical examination revealed an elevated annular erythematous cutaneous lesion

with a paler centre located in the left upper abdominal quadrant (ECM). Admission laboratory findings included thrombocytopaenia (platelet count, $98 \times 10^9/l$) with a mean platelet volume (MPV) of 10.5 fl. The Lyme IgM antibody test was positive at a titre of 1:2 (normal non-reactive). Therapy was begun with doxycycline. Two weeks following initiation of therapy the platelet count had increased to $131 \times 10^9/l$ and the MPV was 11.7 fl. Six weeks later the patient was asymptomatic and the platelet count was $184 \times 10^9/l$ with an MPV of 8.6 fl.

Case 2

A 74 year old woman presented because of a febrile episode occurring 24 hours previously. She had a completely normal physical examination. Two days later she was hospitalized because of increasing malaise, lethargy and a temperature of 100.5°F. A complete blood count at admission showed a white cell count of $10 \times 10^9/l$, haemoglobin of 13.8 g/dl and a haematocrit of 0.412. The platelet count was $43 \times 10^9/l$. An enzyme-linked immunosorbent assay (ELISA) for Lyme disease antibodies (IgG, IgM) was seropositive at a titre of 2.49 (normal range 0–0.9). She was given doxycycline. Bone marrow examination showed normal megakaryocyte numbers. A diagnosis of immune-mediated thrombocytopaenia was made and she was given prednisone 60 mg daily. At a follow-up visit 3 weeks later the platelet count was $140 \times 10^9/l$.

Case 3

A 37 year old part-time gardener sustained a bite on his left arm 2 weeks prior to seeking medical attention. His presenting complaints were joint pains and a rash on the left arm. Physical examina-

Table 1 Summary of clinical findings in patients with thrombocytopaenia and Lyme disease

Case	Age and sex	Skin rash (ECM)	Serological studies	Platelet count ($\times 10^9/l$)	
			specific antibody titres	Presentation	Convalescent
1	26M	Yes	Positive	98	184
2	74F	No	Positive	43	140
3	37M	Yes	N/D	77	230
4	80M	No	Positive	106	—
5	78M	Yes	Negative	70	294
6	16F	Yes	Positive	56	386

tion showed a 4 cm bull's eye lesion on the left arm (ECM). Initial laboratory studies showed a white cell count of $2.3 \times 10^9/l$, a platelet count of $77 \times 10^9/l$ and a haematocrit of 0.45. Doxycycline was prescribed. Three weeks later the platelet count was $230 \times 10^9/l$.

Case 4

A 80 year old man who lived in Northern Westchester County entered the hospital because of a temperature of 104°F associated with a generalized seizure. He had been hospitalized one year previously with an acute illness characterized by hyperpyrexia, diarrhoea and thrombocytopaenia (platelet count $128 \times 10^9/l$). An ELISA (IgM, IgG) for Lyme disease was seropositive at a titre of 2.94. A diagnosis of Lyme disease was made and his illness responded well to intravenous ceftriaxone.

At the time of the second hospital entry his temperature was 103°F . Laboratory examination was significant for the finding of thrombocytopaenia (platelet count $106 \times 10^9/l$). An ELISA (IgM, IgG) for Lyme disease was seropositive at 2.40 (normal range 0–0.9). A diagnosis of acute Lyme disease was made and complete recovery followed therapy with intravenous ceftriaxone.

Case 5

A 78 year old man presented because of a skin rash and fever (temperature 104°F). A dermatology consultant described the rash as erythema chronicum migrans consistent with acute Lyme disease. Laboratory examination showed thrombocytopaenia (platelet count $70 \times 10^9/l$). A Lyme titre done on entry was negative. Therapy with doxycycline was begun. Three days later he was afebrile and his platelet count was $63 \times 10^9/l$. Ten days following discharge he had recovered completely and his platelet count was normal.

Case 6

A 16 year old girl presented with a 2 month history of headaches, weakness, fatigue and aches and pains in the joints. Physical examination revealed a resolving skin lesion (erythema chronicum migrans) on the left lateral chest wall. Laboratory examination of peripheral blood showed a platelet count of $56 \times 10^9/l$ and a MPV of 9.7 fl. Three weeks later the platelet count was $386 \times 10^9/l$ with an MPV of 6.2 fl. A Western immunoblot and flagellum (41 Kd) ELISA for serodiagnosis of Lyme borreliosis was positive.

Discussion

The occurrence of thrombocytopaenia in association with Lyme disease in the patient described in Case 1 prompted memory of a previous patient who had a similar clinical presentation (Case 3). As this association seemed unlikely to be a coincidence we were stimulated to review retrospectively our experience with Lyme disease. We were able to find four additional cases of this association.

The diagnosis of Lyme disease is made by the characteristic appearance of erythema chronicum migrans and a history of possible exposure to *B. burgdorferi*. In this setting serological confirmation is not needed. Although determination of specific antibody titres is a helpful adjunctive test, only a minority of patients with erythema migrans have detectable antibodies to *B. burgdorferi* at the time of presentation and if prompt antibody treatment is administered, seroconversion may not occur.

All six patients described in this report reside in a highly endemic area for Lyme disease in Northern Westchester County, New York. Patients 1 and 3 were both employed in jobs that required considerable outdoor exposure. The characteristic rash of Lyme disease (ECM) was noted upon initial

examination of four patients (Case 1,3,5,6). The two other patients did not have the typical skin rash which either was overlooked or never occurred. Although the unique herald lesion of Lyme disease was not evident in these two subjects their serum samples were positive for antibodies to *B. burgdorferi* and the accompanying clinical symptoms and/or signs were consistent with those described for Lyme disease. A positive serodiagnosis of *B. burgdorferi* infection supported the clinical diagnosis in four of our six patients. (Antibodies to *B. burgdorferi* cross-react with *Treponema pallidum*. All six patients had negative VDRL test results).

Although Lyme borreliosis is the most common arthropod-borne disease of North America and Europe, and its clinical and laboratory manifestations have been well described, the association of thrombocytopaenia with this tick-borne spirochaetal infection has received scant attention in the world literature.⁵ We were unable to find any reports of this association in the English language literature.⁶ We were able to locate two brief case reports linking thrombocytopaenia to Lyme disease in the European literature.^{3,4}

The six patients described in this report represent the first series of patients with coexistent thrombocytopaenia and Lyme disease. All patients had documented thrombocytopaenia during an illness characterized by clinical findings consistent with the diagnosis of Lyme disease. Bone marrow examination was done in Case 2 and the megakaryocytes were normal in number, maturation and morphology.

The mean platelet volume (normal range 7.5–10.0 fl) of patients 2 and 6 was increased during the period of thrombocytopaenia. With normalization of the platelet count the mean platelet volume decreased. These findings are consistent with increased platelet turnover and suggest either platelet consumption or destruction as a cause of the diminished levels of circulating platelets. It is known that the spirochete attaches itself to cell membrane glycoproteins called 'integrins'.⁷ Binding of the spirochete to platelet integrins could conceivably produce platelet damage which eventuates in removal of such platelets from the circulation. Although the marrow findings and the MPV measurements of the patient for whom these values were available support the notion of increased platelet destruction, the precise mechanism of the thrombocytopaenia occurring in these six patients cannot be ascertained from the information available in their hospital records.

Early diagnosis of Lyme disease and institution of appropriate therapy is important as it will significantly decrease the risk of later morbidity (chronic organ damage) which can occur when the disease is unrecognized and hence untreated. The presence of thrombocytopaenia in subjects in endemic areas presenting with a flu-like syndrome should heighten suspicion of Lyme disease (particularly when the pathognomonic rash is absent) and should prompt a more detailed history of possible tick bite and/or objective signs or laboratory findings of Lyme disease.

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